General

Guideline Title

ACR Appropriateness Criteria® pretreatment staging of muscle-invasive bladder cancer.

Bibliographic Source(s)

van der Pol CB, Sahni VA, Eberhardt SC, Oto A, Akin O, Alexander LF, Allen BC, Coakley FV, Froemming AT, Fulgham PF, Hosseinzadeh K, Maranchie JK, Mody RN, Schieda N, Schuster DM, Venkatesan AM, Wang CL, Lockhart ME, Expert Panel on Urologic Imaging. ACR Appropriateness CriteriaÂ® pretreatment staging of muscle-invasive bladder cancer. Reston (VA): American College of Radiology (ACR); 2017. 11 p. [77 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Leyendecker JR, Clingan MJ, Remer EM, Bishoff JT, Blaufox MD, Eberhardt SC, Friedman B, Hartman MS, Hosseinzadeh K, Lazarus E, Lockhart ME, Oto A, Porter C, Sudakoff GS, Verma S, Expert Panel on Urologic Imaging. ACR Appropriateness Criteria® pretreatment staging of invasive bladder cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2012. 12 p. [104 references].

This guideline meets NGC's 2013 (revised) inclusion criteria.

NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report Clinical Practice Guidelines We Can Trust.

Assessment	Standard of Trustworthiness
YES	Disclosure of Guideline Funding Source
	Disclosure and Management of Financial Conflict of Interests

	Guideline Development Group Composition
YES	Multidisciplinary Group
YES	Methodologist Involvement
▮▯▯▯▯	Patient and Public Perspectives
	Use of a Systematic Review of Evidence
▮▮▮▮▮	Search Strategy
▮▮▮▯▯	Study Selection
▮▮▮▮▯	Synthesis of Evidence
	Evidence Foundations for and Rating Strength of Recommendations
▮▮▯▯▯	Grading the Quality or Strength of Evidence
▮▮▮▮▮	Benefits and Harms of Recommendations
▮▮▮▮▮	Evidence Summary Supporting Recommendations
▮▮▮▮▯	Rating the Strength of Recommendations
▮▮▮▮▮	Specific and Unambiguous Articulation of Recommendations
▮▯▯▯▯	External Review
▮▮▮▯▯	Updating

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

Pretreatment Staging of Muscle-Invasive Bladder Cancer

Variant 1: Pretreatment staging of muscle-invasive bladder cancer.

Procedure	Appropriateness Category	Relative Radiation Level
CT abdomen and pelvis without and with IV contrast	Usually Appropriate	☢☢☢☢
X-ray chest	Usually Appropriate	☢
MRI abdomen and pelvis without and with IV contrast	Usually Appropriate	O
CT abdomen and pelvis with IV contrast	Usually Appropriate	☢☢☢☢

Procedure	Appropriateness Category	Relative Radiation Level
MRI pelvis without and with IV contrast	Usually Not Appropriate	O
FDG-PET/CT skull base to mid-thigh	May Be Appropriate	☢☢☢☢
CT chest with IV contrast	May Be Appropriate	☢☢☢
CT chest without IV contrast	May Be Appropriate	☢☢☢
MRI pelvis without IV contrast	May Be Appropriate	O
CT abdomen and pelvis without IV contrast	May Be Appropriate	☢☢☢☢
CT abdomen with IV contrast	Usually Not Appropriate	☢☢☢
CT abdomen without and with IV contrast	Usually Not Appropriate	☢☢☢☢
CT abdomen without IV contrast	Usually Not Appropriate	☢☢☢
CT chest without and with IV contrast	Usually Not Appropriate	☢☢☢
CT pelvis with IV contrast	Usually Not Appropriate	☢☢☢
CT pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢
CT pelvis without IV contrast	Usually Not Appropriate	☢☢☢
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	O
MRI abdomen without IV contrast	Usually Not Appropriate	O
MRI abdomen without and with IV contrast	Usually Not Appropriate	O
MRI head without and with IV contrast	Usually Not Appropriate	O
Tc-99m bone scan whole body	Usually Not Appropriate	☢☢☢
US pelvis (bladder)	Usually Not Appropriate	O
MRI head without IV contrast	Usually Not Appropriate	O
X-ray intravenous urography	Usually Not Appropriate	☢☢☢

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Introduction/Background

The American Cancer Society estimates that in 2017 there will be 79,030 new cases of bladder cancer and 16,870 deaths from the disease in the United States. Bladder cancer has a high tendency toward multifocality at presentation and recurrence after treatment. Urothelial carcinoma (previously known as transitional cell carcinoma) of the bladder is overwhelmingly the most common histologic type of bladder cancer in industrialized nations, accounting for more than 90% of all cases. The median age of patients at diagnosis with bladder cancer in the United States is 73 years. Almost 85% of patients with bladder cancer present with hematuria, which is either gross or microscopic and is usually painless and intermittent.

Bladder urothelial carcinoma spreads by local extension from the urothelium, through the lamina propria, into the muscularis propria or detrusor muscle layer, then to the perivesical fat. It has been estimated that 70% to 85% of bladder urothelial carcinoma is non-muscle-invasive at presentation. Invasion of the muscularis propria and beyond, termed muscle-invasive bladder cancer (MIBC), increases the risk for more

distant spread. The most common metastatic sites for MIBC include lymph nodes, bone, lung, liver, and peritoneum.

Bladder lymph node mapping has demonstrated the complexity and extent of bladder lymphatic drainage. Drainage extends beyond the external iliac vessels and obturator fossa, included in a limited pelvic nodal dissection, to also involve the internal iliacs and common iliac vessels up to the uretero-iliac crossing and occasionally extending to the inferior mesenteric artery. Traditionally, lymph nodes have been considered suspicious based on increased size; however, newer magnetic resonance imaging (MRI) techniques and fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (FDG-PET/CT) can improve malignancy detection in subcentimeter-sized nodes.

Bladder urothelial carcinoma is staged by its extent at presentation and graded as either low grade or high grade. The standard staging system for bladder cancer is the Tumor, Node, Metastasis (TNM) system, which encompasses the status of the primary tumor (T), lymph nodes (N), and metastases (M). Since the last edition of this document, the 8th edition of the American Joint Committee on Cancer (AJCC) Staging Manual was published, which reclassified bladder cancer N staging based on the number of metastatic regional lymph nodes and reclassified common iliac nodes as regional lymph nodes (N3) rather than metastatic disease.

Radical cystectomy with pelvic lymphadenectomy remains the reference standard treatment for MIBC. Neoadjuvant cisplatin-based combination chemotherapy is increasingly being used in these patients, and has been shown to improve disease-specific and overall survival compared with surgery alone. Moving forward, immune-checkpoint inhibitors and molecular-profiling technologies hold potential to fundamentally change management of bladder cancer.

The principal task of imaging is to identify MIBC, extravesical spread, and nodal and distant metastases. The imaging workup begins after the bladder tumor has been identified or confirmed cystoscopically and has been proven by biopsy.

Discussion of Procedures by Variant

Variant 1: Pretreatment Staging of Muscle-invasive Bladder Cancers

CT Pelvis

In many centers, abdominal imaging, usually with contrast, will be obtained in conjunction with pelvis/bladder imaging as part of complete staging. For details regarding bladder cancer detection, refer to the National Guideline Clearinghouse (NGC) summaries of the ACR Appropriateness Criteria® Hematuria and Post-treatment surveillance of bladder cancer.

The contribution of CT for bladder cancer staging includes identification of multifocal disease, extravesical extension, adenopathy, and metastases. CT demonstrates bulky thickening of the bladder wall, perivesical extension, lymph node enlargement, and distant metastases very well. CT cannot distinguish inflammatory post-treatment edema or fibrosis from tumor and cannot assess depth of invasion of the bladder wall. CT is also unable to detect microscopic or small-volume extravesical tumor extension and metastases in nonenlarged lymph nodes.

One study reviewed 437 cases in the literature using CT to stage bladder urothelial carcinoma. Overall accuracy ranged from 40% to 85%, with correct staging of nodes and metastases ranging from 82% to 97%. For extravesical extension, accuracy ranged from 40% to 92% with a mean of 74%. Another study found overall accuracy of 55%, with 39% understaging and 21% false negative for extravesical spread. In a retrospective review of 276 patients researchers found that CT accuracy for predicting pathological tumor stage was 49% and accuracy for predicting lymph node metastases was 54%, and concluded that multidetector CT had little impact on decision making for local treatment of MIBC during radical cystectomy. Another study by the same group found that there was significant interobserver variability in CT findings that might contribute to the limited accuracy of CT in the detection of extravesical tumor spread, infiltration of extravesical organs, and lymph node involvement.

In a prospective study of 63 patients, researchers showed that CT T-stage could help surgeons determine the extent of pelvic lymph node dissection required, with lower-stage tumors requiring less extensive nodal dissection, reducing the risk of complications. Another study found that the sensitivity of CT imaging for the detection of lymph node metastases was low, while high values for specificity were achieved.

In addition to multidetector CT, the use of multiplanar reformation, 3-D reconstruction, and creation of images mimicking traditional cystoscopy (a technique often referred to as virtual cystoscopy) have been assessed in the literature. Using multiplanar reformation, a group of researchers found an overall accuracy of 88% in CT staging of all stages of bladder cancer and, more specifically, 77% for Ta-T2 lesions and 95% for T3-T4 lesions. Pathologic lymph nodes were confirmed in six of seven cases. Multiplanar reformation was shown to be useful in evaluating the origin and extent of extravesical invasion as well as the tumor's relationship to the ureter.

CT Abdomen

Abdominal CT can be acquired at the same time as a pelvic CT in one continuous scan and can be useful for the detection of abdominal adenopathy and metastases. Researchers looked at 201 patients with biopsy-proven bladder urothelial carcinoma and a CT whole-body staging at time of diagnosis for evaluation of distant metastatic disease. Of these patients, 6% had distant metastatic spread, most commonly retroperitoneal lymph nodes. None of the patients with non-muscle-invasive bladder cancer had metastases. The detection of peritoneal metastases from bladder cancer with CT has also been described. In one study, CT findings of peritoneal metastases were found in 8 of 105 patients and were indicative of a poor prognosis. Another study found peritoneal metastasis in 24 of 150 patients, occurring more frequently in those with atypical histology including squamous cell carcinoma, adenocarcinoma, small cell carcinoma, and undifferentiated tumors.

An estimated 2% to 4% of patients with urothelial carcinoma of the bladder will also develop upper-tract disease, thus requiring evaluation of the entire urothelium. An abdomen-pelvis CT urogram protocol can aid in the detection of upper tract disease. The widespread use of CT urography and emerging use of MR urography have essentially replaced intravenous urography (IVU) for evaluating the renal collecting systems and ureters. Advantages of a cross-sectional technique, such as CT urography, includes the ability to directly visualize small masses, which may be obscured by contrast material or overlying bowel gas on excretory urography, to identify focal wall thickening, and to distinguish otherwise nonspecific filling defects as enhancing tumor versus nonenhancing calculi or blood clots. CT and MR urography offer the ability to potentially assess a nonfunctioning/obstructed kidney that would not excrete the contrast medium required for excretory urography. These strengths compelled one set of researchers to conclude "CT urography should be considered as the initial examination for the evaluation of patients at high risk for upper urinary tract urothelial carcinoma." Furthermore, another group of researchers concluded "the consensus is that CT urography can detect many more bladder cancers than excretory urography."

MRI Pelvis

MRI is the best imaging modality for locally staging bladder cancer. The soft tissue contrast resolution of MRI makes it more optimal than CT for detecting bladder cancer invasion of the detrusor muscle, perivesical tissues, and adjacent organs. The addition of newer sequences has been shown to further improve local staging accuracy and detection of malignant regional lymph nodes. One study compared the staging accuracy of diffusion-weighted imaging (DWI) to T2-weighted sequences, finding DWI superior in staging organ-confined tumors ≤T2 disease. Likewise, another study found that DWI added information to T2-weighted images alone when evaluating the T-stage of bladder cancer, significantly improving accuracy, specificity, and area under the receiver operating curves, with best results from combining T2-weighted images. In a study that included both bladder and prostate cancer, a combination of DWI signal intensity relative to groin lymph nodes, as well as morphologic criteria at T2-weighted imaging, was used to identify malignant nodes. The researchers reported sensitivity of 61% to 94%, specificity of 90% to 99%, and accuracy of 83% to 96% for malignant node detection on a per-patient basis and a sensitivity of 55% to 87%, specificity of 94% to 100%, and accuracy of 88% to 96% for malignant node detection on

a per-pelvic side basis.

The addition of gadolinium-based contrast has been shown to further improve the local staging accuracy of bladder cancer on MRI. Researchers conducted a prospective study on 122 patients using gadolinium-enhanced MRI. They found that MRI had 88% sensitivity, 48% specificity, and 74% accuracy in differentiating organ-confined from non–organ-confined bladder cancer, as well as 41% sensitivity, 92% specificity, and 80% accuracy for the detection of positive nodal disease. Interobserver agreement for T and N staging was moderate, similar to other studies which showed moderate-to-good agreement. Multiple other publications report the sensitivity and specificity of MRI for differentiating non-muscle-invasive from muscle invasive tumors at 78% to 98% and 82% to 100% and the sensitivity and specificity for differentiating organ-confined from non–organ-confined tumors at 90% to 94% and 60% to 94%. The combination of dynamic contrast-enhanced imaging with DWI and T2-weighted imaging is referred to as multiparametric MRI, which is likely the most optimal MRI technique for the local staging of bladder cancer.

MRI has been shown to have a tendency towards overestimation of T-stage, with anywhere from 32% to 55% of patients having a reduced T-stage at resection. This could, in part, be due to comparison to transurethral resection of bladder tumor specimens as the reference standard in some studies, which has been shown to underestimate local staging in up to 40% of cases.

Noting that MRI has better sensitivity and specificity than CT for local staging, a group of researchers stated that MRI and CT have similar accuracy for detecting perivesical fat invasion and that the most notable advantage of MRI is its apparent ability to differentiate between superficial and deep invasion of the bladder wall. One study concluded that MRI is the best technique for staging invasive tumors, as it was slightly better than or equal to CT at differentiating T3a from T3b lesions and superior to CT for detecting tumors at the bladder dome or base. In deeply infiltrating tumors (stages T3b-T4b), the researchers asserted that MRI "is generally agreed to be the most accurate staging technique," and "when MRI is available, CT is no longer needed." One review contends, "MRI is superior (to CT) for evaluation of the depth of invasion in the bladder wall." The authors go on to say that "both modalities continue to have difficulties in determining whether perivesical changes are related to tumor or inflammation from the previous transurethral biopsy." However, emerging data regarding the addition of DWI to standard pelvic MRI may help differentiate treatment response and residual/recurrent disease.

MRI has been reported to be more precise in the identification and localization of lymph nodes in the setting of pelvic malignancy when compared to CT, in particular for smaller nodes ranging in size from 1 to 5 mm. Lymph node metastases in patients with tumors <T3 are rare, but if deep muscle layers are involved (T2b) or if extravesical invasion is seen, the incidence of lymph node metastases rises to 20% to 30% and 50% to 60%, respectively. If a lymph node is considered to contain metastasis, a fine-needle aspiration biopsy should be considered.

As with CT, there has also been interest in 3-D rendering techniques with MR data sets (including multiplanar reconstructions and creation of cystoscopic-like images) as a replacement for traditional cystoscopy and to assist in staging. These techniques are mostly experimental at present.

MRI Abdomen

Abdomen MRI and, in particular, MR urography may be performed for nodal, upper-tract, and metastatic staging in conjunction with dedicated pelvic imaging for local bladder staging. Non-contrast enhanced MR urography can be used to assess the renal collecting systems and ureters using a heavily T2-weighted sequence when iodinated contrast is contraindicated, such as in those with a severe allergy to iodinated contrast, in pregnancy, and in pediatric patients.

IVU

The widespread use of CT urography and emerging use of MR urography have essentially replaced IVU for evaluation of the urothelium in the renal collecting systems and ureters. Sensitivity of excretory urography to detect upper urinary tract lesions is reportedly 50% to 70%. However, a study comparing the accuracy of detection and localization of upper urinary tract urothelial carcinoma with CT urography versus

excretory urography favored CT urography with per-patient sensitivity, specificity, and overall accuracy rates of 93.5%, 94.8%, and 94.2%, respectively, compared with 80.4%, 81.0%, and 80.8%, respectively, for excretory urography.

Retrograde ureteropyelography, often performed at the time of cystoscopy, is also excellent for detailed study of the urothelium.

FDG-PET/CT

Conventional PET is limited for the local staging of bladder tumors because of high FDG activity in excreted urine. The current body of literature regarding the ability of FDG-PET to stage bladder cancer suggests it improves sensitivity for diagnosing nodal and metastatic disease, particularly when combined with CT (FDG-PET/CT).

A study of 233 patients found the sensitivity and specificity of CT for pelvic lymph node involvement was 45% and 98%, respectively. Using PET/CT, the sensitivity for pelvic lymph node involvement increased to 69% with a 3% reduction in specificity to 95%. In a prospective study of 25 patients, in nine patients who had positive lymph nodes for metastases on histopathology, CT and PET/CT scans had a sensitivity of 44% and 78%, respectively. Other authors have found FDG-PET/CT sensitivity for detection of nodal metastases to range between 47% and 56% and specificity to range between 93% and 98%, with specificity often slightly lower than CT.

One research group retrospectively analyzed 70 bladder cancer patients staged with FDG-PET/CT before radical cystectomy and found that sensitivity, specificity, and accuracy were 55%, 90%, and 84% for FDG-PET alone; 46%, 92%, and 84% for CT using an 8-mm cutoff; and 27%, 97%, and 86% for CT using a 10-mm cutoff. Combined FDG-PET/CT resulted in a nonsignificant increase of diagnostic accuracy using a cutoff >8 mm for lymph node evaluation (64%, 86%, and 83%, respectively).

Another study found that FDG-PET detected metastatic disease outside of the pelvis with a sensitivity of 54% compared with 41% for CT, while both PET/CT and CT had similar specificities of 97% and 98%, respectively. Another group of researchers prospectively evaluated FDG-PET/CT for staging of MIBC in patients with no evidence of metastatic disease by conventional staging methods, reporting a sensitivity of 70%, specificity of 94%, PPV of 78%, and a NPV of 91% for PET/CT among this population. In this study, treatment approach was altered in two patients, one receiving neoadjuvant chemotherapy and a second with widespread metastatic disease receiving palliative chemotherapy.

FDG-PET/CT results can affect clinical decisions in patients with bladder cancer. Researchers prospectively looked at patients with bladder cancer through the national oncology PET registry and conducted a clinical impact analysis. Physicians surveyed noted that PET/CT found more disease in 40% of patients and less disease in 18% of patients. Overall, PET/CT results changed the treatment plan in 68% of patients. Even after applying an imaging-adjusted impact for patients in whom a different imaging test such as CT or MRI may have led to the same management strategy, PET/CT still changed the treatment plan in 47% of patients. In another study, researchers prospectively assessed 103 patients with high-risk MIBC who underwent FDG-PET/CT in addition to CT, and found that FDG-PET/CT findings led to an altered provisional treatment plan in 27% of patients. Another study of 96 consecutive patients with bladder cancer found that FDG-PET/CT provided additional staging information that influenced the treatment of MIBC in almost 20% of cases.

^{11}C-choline PET is mostly experimental at present. When compared with CT, ^{11}C-choline PET promises increased accuracy of lymph node staging and may avoid false-positive results for lymph nodes due to reactive hyperplasia when compared with CT. The current literature suggests that ^{11}C-choline PET/CT has a sensitivity of 42% to 59% and specificity of 84% to 90% for detecting nodal disease. Researchers compared ^{11}C-choline PET/CT with FDG-PET/CT for a total of 51 lesions in 20 consecutive patients with bladder cancer. The PPV for all detected lesions was 85% for ^{11}C-choline PET/CT and 91% for FDG-PET/CT. The corresponding PPVs for extravesical lesions were 79% and 88%, respectively. FDG-PET/CT correctly identified four extravesical metastases missed by ^{11}C-choline PET/CT. The authors concluded

that ^{11}C-choline PET/CT had no advantage compared to FDG-PET/CT in the detection of metastatic bladder cancer.

Radiography

All patients with MIBC need pulmonary evaluation. The chest radiograph is an effective and low-morbidity screen.

CT Chest

Patients with findings on chest radiographs and those thought to be at high risk should have chest CT, as is recommended in other guidelines. Original research comparing the usefulness of chest radiographs to chest CT in this patient population is lacking.

Bone Scan

The incidence of metastases in bladder cancer patients increases with tumor stage at time of diagnosis. A 4.6% positive rate was found in 458 bone scan studies, with only a 2.8% true-positive rate. Because therapy was affected in only 0.9%, the conclusion was that scintigraphy has "no place in the routine preoperative staging of bladder carcinoma." Another study of 91 patients with precystectomy bone scan concluded that, in the absence of additional investigations such as MRI, "the findings of a routine preoperative bone scan are usually unable to identify patients with bladder cancer of stage ≥T2 who will not be cured by total cystectomy." Nonetheless, when one considers only those patients with MIBC, the likely positivity of bone scanning increases, as does its importance in guiding proper management and avoiding unnecessary radical surgery and expense. One study looking at 179 consecutive patients with bladder cancer found that 14.5% had bone metastasis at presentation; however, 61.5% of those with metastatic disease had deep muscle invasion, compared with 19.2% demonstrating superficial muscle invasion, and 7.7% demonstrating no muscle invasion, leading the authors to advocate the routine use of bone scan in patients with MIBC. Otherwise, bone scanning may be limited to patients with bone pain and/or elevated levels of serum alkaline phosphatase. Further evaluation with radiographs and/or MRI can be helpful, and, if necessary, guided-needle biopsy can be definitive.

US

The distended bladder is a superb acoustic window. In 214 new cases of bladder urothelial carcinoma with pathological correlation, researchers reported overall accuracy of 79% in local staging with transabdominal ultrasound (TAUS). They had 10% overstaging and 12% understaging. However, TAUS is limited in visualization beyond the bladder wall and cannot reliably detect nodal enlargement. TAUS is also less accurate for detecting stage T3 and T4 disease compared to T1 and T2 disease. Some investigators have correlated sonographically determined contact length and height-to-length ratio with depth of tumor invasion at TAUS. A contact length of >41.5 mm and a height-to-length ratio of <0.605 were calculated as cutoff values for differentiating non-muscle-invasive and invasive tumors.

Three-dimensional US rendering is yet another newer diagnostic tool with potential to aid in discriminating nonmuscle-invasive from muscle-invasive tumors. Contrast-enhanced sonography has also been shown to better differentiate MIBC from non-muscle-invasive bladder neoplasms.

Aside from TAUS, other approaches include transurethral US and endoluminal US, also known as intravesical US. One study reported an overall accuracy of 97% in diagnosing and staging bladder tumors with transurethral US in 104 patients: 96% for stage Ta-T1 lesions, 100% for T2 lesions, 92% for T3 lesions, and 100% for T4 lesions. Endoluminal US uses a miniature, high-frequency transducer introduced by a rigid cystoscope for intravesical evaluation.

MRI Head

Neurologic complications directly related to bladder cancer are rare and are usually the result of local extension, for example to the lumbosacral plexus, rather than brain metastases. One study of the metastatic pattern of MIBC found the brain to be the ninth most common site of metastatic disease, occurring in 5% of patients. Therefore, MRI of the head is not recommended for asymptomatic patients.

Summary of Recommendations

The most appropriate imaging studies for pretreatment staging of muscle-invasive bladder cancer are; (1) CT abdomen and pelvis without and with contrast (CT urography), (2) CT abdomen and pelvis with IV contrast, (3) MRI abdomen and pelvis without and with IV contrast (MR urography), (4) MRI pelvis without and with IV contrast, and (5) chest radiographs. The imaging studies listed above are complementary; meaning more than one can be performed.

Abbreviations

CT, computed tomography
FDG-PET, fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography
IV, intravenous
MRI, magnetic resonance imaging
TAUS, transabdominal ultrasound
Tc-99m, technetium 99 metastable
US, ultrasound

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."		

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

Muscle-invasive bladder cancer

Guideline Category

Diagnosis

Evaluation

Clinical Specialty

Family Practice

Internal Medicine

Nuclear Medicine

Oncology

Radiation Oncology

Radiology

Urology

Intended Users

Advanced Practice Nurses

Health Care Providers

Hospitals

Managed Care Organizations

Physician Assistants

Physicians

Students

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of imaging procedures for pretreatment staging of muscle-invasive bladder cancer

Target Population

Patients with muscle-invasive bladder cancer

Interventions and Practices Considered

1. X-ray
    - Chest
    - Intravenous (IV) urography
2. Computed tomography (CT)
    - Abdomen and pelvis without and with IV contrast
    - Abdomen and pelvis with IV contrast
    - Abdomen and pelvis without IV contrast
    - Abdomen with IV contrast
    - Abdomen without and with IV contrast
    - Abdomen without IV contrast
    - Chest without and with IV contrast
    - Chest without IV contrast
    - Chest with IV contrast
    - Pelvis with IV contrast

    - Pelvis without and with IV contrast
    - Pelvis without IV contrast
3. Magnetic resonance imaging (MRI)
    - Pelvis without and with IV contrast
    - Pelvis without IV contrast
    - Abdomen without and with IV contrast
    - Abdomen without IV contrast
    - Abdomen and pelvis without and with IV contrast
    - Abdomen and pelvis without IV contrast
    - Head without IV contrast
    - Head without and with IV contrast
4. Technetium (Tc)-99m bone scan, whole body
5. Fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET)/CT, skull base to mid-thigh
6. Ultrasound (US), pelvis (bladder)

Major Outcomes Considered

- Utility of imaging procedures in pretreatment staging of muscle-invasive bladder cancer
- Sensitivity, specificity, and accuracy of staging procedures
- Positive and negative predictive values of staging procedures

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Summary

Of the 103 citations in the original bibliography, 41 were retained in the final document.

A literature search was conducted in May 2015, July 2016, and June 2017 to identify additional evidence published since the *ACR Appropriateness Criteria® Pretreatment Staging of Muscle-Invasive Bladder Cancer* topic was finalized. Using the search strategies described in the literature search companion (see the "Availability of Companion Documents" field), 92 unique articles were found. Twenty articles were added to the bibliography. The remaining articles were not used due to either poor study design, the articles were not relevant or generalizable to the topic, or the results were unclear or biased.

The author added 13 citations from bibliographies, Web sites, or books that were not found in the literature searches, including 1 article outside of the search date ranges.

Three citations are supporting documents that were added by staff.

See also the American College of Radiology (ACR) Appropriateness Criteria® literature search process document (see the "Availability of Companion Documents" field) for further information.

Number of Source Documents

Of the 103 citations in the original bibliography, 41 were retained in the final document. The literature searches conducted in May 2015, July 2016, and June 2017 found 20 articles that were added to the bibliography. The author added 13 citations from bibliographies, Web sites, or books that were not found in the literature searches, including 1 article outside of the search date ranges. Three citations are supporting documents that were added by staff.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Definitions of Study Quality Categories

Category 1 - The study is well-designed and accounts for common biases.

Category 2 - The study is moderately well-designed and accounts for most common biases.

Category 3 - The study has important study design limitations.

Category 4 - The study or source is not useful as primary evidence. The article may not be a clinical study, the study design is invalid, or conclusions are based on expert consensus.

> The study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
>
> *Or*
>
> The study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
>
> *Or*
>
> The study is an expert opinion or consensus document.

Category M - Meta-analysis studies are not rated for study quality using the study element method because the method is designed to evaluate individual studies only. An "M" for the study quality will indicate that the study quality has not been evaluated for the meta-analysis study.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author assesses the literature then drafts or revises the narrative summarizing the evidence found in the literature. American College of Radiology (ACR) staff drafts an evidence table based on the analysis of the selected literature. These tables rate the study quality for each article included in the narrative.

The expert panel reviews the narrative, evidence table and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the variant table(s). Each individual panel member assigns a rating based on his/her interpretation of the available

evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Overview

The purpose of the rating rounds is to systematically and transparently determine the panels' recommendations while mitigating any undue influence of one or more panel members on another individual panel member's interpretation of the evidence. The panel member's rating is determined by reviewing the evidence presented in the Summary of Literature Review and assessing the risks or harms of performing the procedure or treatment balanced with the benefits of performing the procedure or treatment. The individual panel member ratings are used to calculate the median rating, which determines the panel's rating. The assessment of the amount of deviation of individual ratings from the panel rating determines whether there is disagreement among the panel about the rating.

The process used in the rating rounds is a modified Delphi method based on the methodology described in the RAND/UCLA Appropriateness Method User Manual.

The appropriateness is rated on an ordinal scale that uses integers from 1 to 9 grouped into three categories (see the "Rating Scheme for the Strength of the Recommendations" field).

Determining the Panel's Recommendation

> Ratings represent an individual's assessment of the risks and benefits of performing a specific procedure for a specific clinical scenario on an ordinal scale. The recommendation is the appropriateness category (i.e., "Usually appropriate," "May be appropriate," or "Usually not appropriate").
> The appropriateness category for a procedure and clinical scenario is determined by the panel's median rating without disagreement (see below for definition of disagreement). The panel's median rating is calculated after each rating round. If there is disagreement after the second rating round, the rating category is "May be appropriate (Disagreement)" with a rating of "5" so users understand the group disagreed on the final recommendation. The actual panel median rating is documented to provide additional context.
> Disagreement is defined as excessive dispersion of the individual ratings from the group (in this case, an Appropriateness Criteria [AC] panel) median as determined by comparison of the interpercentile range (IPR) and the interpercentile range adjusted for symmetry (IPRAS). In those instances when the IPR is greater than the IPRAS, there is disagreement. For a complete discussion, please refer to chapter 8 of the RAND/UCLA Appropriateness Method User Manual.
> Once the final recommendations have been determined, the panel reviews the document. If two thirds of the panel feel a final recommendation is wrong (e.g., does not accurately reflect the evidence, may negatively impact patient health, has unintended consequences that may harm health care, etc.) and the process must be started again from the beginning.

For additional information on the ratings process see the Rating Round Information document (see the "Availability of Companion Documents" field).

Additional methodology documents, including a more detailed explanation of the complete topic development process and all ACR AC topics can be found on the ACR Web site (see also the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current medical evidence literature and the application of the RAND/UCLA appropriateness method and expert panel consensus.

Summary of Evidence

Of the 77 references cited in the *ACR Appropriateness Criteria® Pretreatment Staging of Muscle-Invasive Bladder Cancer* document, 8 are categorized as therapeutic references including 1 well-designed study, 1 good-quality study, and 1 quality study that may have design limitations. Additionally, 69 references are categorized as diagnostic references including 2 well-designed studies, 22 good-quality studies, and 19 quality studies that may have design limitations. There are 31 references that may not be useful as primary evidence.

Although there are references that report on studies with design limitations, 26 well-designed or good-quality studies provide good evidence.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Magnetic resonance imaging (MRI) is the best imaging modality for locally staging bladder cancer. The soft tissue contrast resolution of MRI makes it more optimal than computed tomography (CT) for detecting bladder cancer invasion of the detrusor muscle, perivesical tissues, and adjacent organs. The addition of newer sequences has been shown to further improve local staging accuracy and detection of malignant regional lymph nodes.
- The most notable advantage of MRI for local staging is its apparent ability to differentiate between superficial and deep invasion of the bladder wall.

Potential Harms

- Magnetic resonance imaging (MRI) has been shown to have a tendency towards overestimation of T-stage, with anywhere from 32% to 55% of patients having a reduced T-stage at resection.
- False-positive and false-negative imaging results

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults. Additional information regarding radiation dose assessment for imaging examinations can be found in the American College of Radiology (ACR) Appropriateness Criteria® Radiation Dose Assessment Introduction document (see the "Availability of Companion Documents" field).

Contraindications

Contraindications

Iodinated contrast is contraindicated in patients with a severe allergy to iodinated contrast, in pregnancy, and in pediatric patients.

Qualifying Statements

Qualifying Statements

- The American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the

selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

- ACR seeks and encourages collaboration with other organizations on the development of the ACR Appropriateness Criteria through society representation on expert panels. Participation by representatives from collaborating societies on the expert panel does not necessarily imply society endorsement of the final document.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

van der Pol CB, Sahni VA, Eberhardt SC, Oto A, Akin O, Alexander LF, Allen BC, Coakley FV, Froemming AT, Fulgham PF, Hosseinzadeh K, Maranchie JK, Mody RN, Schieda N, Schuster DM, Venkatesan AM, Wang CL, Lockhart ME, Expert Panel on Urologic Imaging. ACR Appropriateness CriteriaÂ® pretreatment staging of muscle-invasive bladder cancer. Reston (VA): American College of Radiology (ACR); 2017. 11 p. [77 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2017

Guideline Developer(s)

American College of Radiology - Medical Specialty Society

Source(s) of Funding

The funding for the process is assumed entirely by the American College of Radiology (ACR). ACR staff support the expert panels through the conduct of literature searches, acquisition of scientific articles, drafting of evidence tables, dissemination of materials for the Delphi process, collation of results, conference calls, document processing, and general assistance to the panelists.

Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Urologic Imaging

Composition of Group That Authored the Guideline

Panel Members: Christian B. van der Pol, MD (*Research Author*); V. Anik Sahni, MD (*Principal Author*); Steven C. Eberhardt, MD (*Panel Chair*); Aytekin Oto, MD (*Panel Vice-chair*); Oguz Akin, MD; Lauren F. Alexander, MD; Brian C. Allen, MD; Fergus V. Coakley, MD; Adam T. Froemming, MD; Pat F. Fulgham, MD; Keyanoosh Hosseinzadeh, MD; Jodi K. Maranchie, MD; Rekha N. Mody, MD; Nicola Schieda, MD; David M. Schuster, MD; Aradhana M. Venkatesan, MD; Carolyn L. Wang, MD; Mark E. Lockhart, MD, MPH (*Specialty Chair*)

Financial Disclosures/Conflicts of Interest

Disclosing Potential Conflicts of Interest and Management of Conflicts of Interest

An important aspect of committee operations is the disclosure and management of potential conflicts of interest. In 2016, the American College of Radiology (ACR) began an organization-wide review of its conflict of interest (COI) policies. The current ACR COI policy is available on its Web site. The Appropriateness Criteria (AC) program's COI process varies from the organization's current policy to accommodate the requirements for qualified provider-led entities as designated by the Centers for Medicare and Medicaid Services' Appropriate Use Criteria (AUC) program.

When physicians become participants in the AC program, welcome letters are sent to inform them of their panel roles and responsibilities, including a link to complete the COI form. The COI form requires disclosure of all potential conflicts of interest. ACR staff oversees the COI evaluation process, coordinating with review panels consisting of ACR staff and members, who determine when there is a conflict of interest and what action, if any, is appropriate. In addition to making the information publicly available, management may include exclusion from some topic processes, exclusion from a topic, or exclusion from the panel.

Besides potential COI disclosure, AC staff begins every committee call with the conflict of interest disclosure statement on the Web site reminding members to update their COI forms. If any updates to their COI information have not been submitted, they are instructed not to participate in discussion where an undisclosed conflict may exist.

Finally, all ACR AC are published as part of the Journal of the American College of Radiology (JACR)

electronic supplement. Those who participated on the document and are listed as authors must complete the JACR process that includes completing the International Committee of Medical Journal Editors (ICMJE) COI form which is reviewed by the journal's staff/publisher.

Dr. Oto reports grants from Philips, grants from Guerbet, grants from Profound Healthcare, and other from Profound Healthcare, outside the submitted work; Dr. Lockhart is Deputy Editor, Journal of Ultrasound in Medicine; Member, ACR Commission on Ultrasound; Book Author, Oxford Publishers.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Leyendecker JR, Clingan MJ, Remer EM, Bishoff JT, Blaufox MD, Eberhardt SC, Friedman B, Hartman MS, Hosseinzadeh K, Lazarus E, Lockhart ME, Oto A, Porter C, Sudakoff GS, Verma S, Expert Panel on Urologic Imaging. ACR Appropriateness Criteria® pretreatment staging of invasive bladder cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2012. 12 p. [104 references].

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the American College of Radiology (ACR) Web site .

Availability of Companion Documents

The following are available:

ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2017. Available from the American College of Radiology (ACR) Web site .

ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2015 Feb. 1 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Evidence table development. Reston (VA): American College of Radiology; 2015 Nov. 5 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Topic development process. Reston (VA): American College of Radiology; 2015 Nov. 2 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Rating round information. Reston (VA): American College of Radiology; 2017 Sep. 5 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Radiation dose assessment introduction. Reston (VA): American College of Radiology; 2018. 4 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Manual on contrast media. Reston (VA): American College of Radiology; 2017. 125 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Procedure information. Reston (VA): American College of Radiology; 2017 Mar. 4 p. Available from the ACR Web site .

ACR Appropriateness Criteria® pretreatment staging of muscle-invasive bladder cancer. Evidence table. Reston (VA): American College of Radiology; 2017. 32 p. Available from the ACR Web site .

ACR Appropriateness Criteria® pretreatment staging of muscle-invasive bladder cancer. Literature search. Reston (VA): American College of Radiology; 2017. 2 p. Available from the ACR Web site .

Patient Resources

None available

NGC Status

This summary was completed by ECRI on May 6, 2001. The information was verified by the guideline developer as of June 29, 2001. This summary was updated by ECRI on September 8, 2004. The updated information was verified by the guideline developer on October 8, 2004. This NGC summary was updated by ECRI on February 7, 2006. This summary was updated by ECRI Institute on May 17, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Gadolinium-based contrast agents. This summary was updated by ECRI Institute on June 20, 2007 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This NGC summary was updated by ECRI Institute on December 3, 2007 and on June 17, 2010. This summary was updated by ECRI Institute on January 13, 2011 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This summary was updated by ECRI Institute on May 9, 2013. This summary was updated by ECRI Institute on June 13, 2018. The guideline developer agreed to not review the content.

This NEATS assessment was completed by ECRI Institute on May 30, 2018.

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